The specification has been amended to update continuation data concerning application Serial No. 07/817,430. The specification has been further amended to add Sequence ID Nos. in the appropriate places.

Claims 1-4 have been amended to clarify that the amino acids recited are in sequence and to call for a Sequence ID No. Claims 1-4 have also been amended to substitute the term "has" for "comprises". Claims 5 and 6 have been corrected to call for Figure 14. Claim 7 has been amended for clarification of the 61 amino acids. Basis for claim 7 is found on page 11, lines 9-15. Claim 8 has been amended for clarification and to call for Sequence ID Nos. Claims 12 and 13 have been newly added. Basis for claim 12 is found in Figure 14. The features of claim 13 were previously called for in claims 1-11.

Rejections under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 1-11 under 35 U.S.C. §112, first paragraph. Applicants traverse the rejection of the claims on this ground, as detailed below.

I. The Examiner has rejected claims 1-10 as being enabled only for an Escherichia coli, the RT of which synthesizes msDNA. Applicants submit the claims are fully enabled as claimed.

The specification teaches that one skilled in the art may screen a bacterium, any bacterium, to determine whether the bacterium makes msDNA. See page 32, line 14, to page 34, line 22.

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

If the bacterium makes msDNA, it must likewise produce a reverse transcriptase. See page 32, line 20. The application teaches that the RT is essential for the synthesis of msDNA. There is no msDNA in the absence of the bacterial RT.

Thus, the test for the presence of RT in a bacterium is by testing for the presence of msDNA. If msDNA is present, then RT must be present because RT is essential for the production of msDNA. The specification teaches two assays for the determination of the presence of msDNA.

The Examiner, in the bridging paragraph of pages 3-4 of the Office Action, has apparently misread the claims in placing virtual exclusive weight on the amino acid residues, while ignoring the remainder of the claims, which recites the limitation that on RTs are claimed which have the ability to synthesize msDNA. The law is clear that an Examiner must consider all limitations in a claim. Once it is determined that a bacterium produces the reverse transcriptase, which is determined by the presence of msDNA, the RT can be isolated and purified by the method taught in Example 3 on pages 39-40.

The specification teaches that many different genera of bacteria were tested in accordance with the invention. See page 33, lines 8-19, and Figure 20. One of the screening methods taught in the specification was used to determine the presence of msDNA, and therefore RT, in a collection of rhizobial isolates. See page 35, lines 9-19, and Figure 21.

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

Applicants submit, therefore, that the specification is adequately enabling for screening any bacterium, including *Escherichia spp.*, for the presence of msDNA, and thus for RT, and for isolating and purifying the RT.

The applicable standard for §112, first paragraph, is that the claims are enabled when the invention can be practiced without undue experimentation. Applicants submit that they have met this standard.

The Examiner erroneously states that the specification teaches that:

> once an RT is determined to exist, it must be identified and screened. Then any resultant RT must be produced and identified.

To the contrary, once an RT is determined to exist by determining the existence of msDNA, the RT is then isolated and purified in accordance with the teaching of the specification.

The specification further teaches that the four amino acids called for in claim 1 are highly conserved in RTs. The RT, however, may be determined, isolated, and purified irrespective of these four amino acids. The method taught in the application in Example 3, on pages 39-40, for isolating and purifying the RT is based on RT activity and so is independent of sequence. Accordingly, the RT of the invention is adequately enabled with respect to any bacterium, irrespective of the amino acid sequence called for in claim 1, and of those called for in claims 2-4. The claims calling for amino acid sequences add additional features of

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

the RT, with which one may further characterize the RT, once isolated.

Moreover, the order of the amino acid sequences called for in claims 1-4 is immaterial. The sequences are present and may, for example, be used to further define the RT once isolated and purified.

Accordingly, Applicants submit that new claim 13, which is an independent claim calling for a bacterial RT which is capable of synthesizing msDNA, is adequately enabled. Claim 1, which calls for a specified amino acid sequence as part of the RT, is now dependent from claim 13.

Applicants submit that the claims are adequately enabled for a bacterium of any species, including *Escherichia spp.*, and respectfully request the Examiner to withdraw the rejection of the claims on this ground.

II. The Examiner has rejected claim 8 as not being enabled because the claim calls for an RT that "comprises a sequence of amino acid residues from any of the amino acids found in Figure 14." The claim has been amended to indicate that it is the entire amino acid sequence, selected from the group of 7 amino acid sequences shown in Figure 14, which is called for in claim 8. Thus, the amendments to claim 8 obviate the concern of the Examiner that the claim calls for a sequence which:

> encompasses any from 2-3 short fragments from Figure 14 to a whole sequence, or many portions of any of the sequences together.

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

As is evident, armed with the knowledge of the amino acid sequence of an enzyme, one skilled in the art would be able to isolate the enzyme by various means, including by means of one or more specific probes. Further, the specification teaches the isolation and purification of a bacterial RT. See Example 3, pages 39-40. Once purified, one skilled in the art is capable of determining the sequence of the RT. The specification also teaches a reference, Lampson et al., which teaches an additional means to isolate and purify an RT. See page 40, lines 16-18.

Thus, Applicants submit that claim 8, as amended, is fully enabled, and respectfully request the Examiner to withdraw the rejection of claim 8 on this ground.

III. The Examiner has rejected claims 9-11 for not being enabled because the screening test is

> not a means to enable one to produce the invention,

but rather, the test

> is a description of a means for one in the art to test the activity of an RT enzyme <u>once it is found</u>. (emphasis in the original).

The Examiner has miscomprehended the nature of the screening test as taught in the specification, and as claimed in claims 9-11.

Claims 9-11 call for a screening test, known as the reverse transcriptase extension <u>in vitro</u> screening test, to

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

determine whether a bacterium is capable of synthesizing msDNA. As recited in claim 9, this test indicates the presence or absence of msDNA in the tested bacterium. The screening test is disclosed in two references which are incorporated by reference in the specification on pages 32-33, bridging paragraph.

The methodology of the screening test, as set forth in claim 11, is treating a preparation of total RNA extracted from the bacterium with a reverse transcriptase (RT) in the presence of a radiolabelled deoxynucleotide. If msDNA is present in the total RNA, radiolabelled msDNA will be produced by the action of the RT, which msDNA can be detected by electrophoresis.

The Examiner has understood the test to indicate the activity of the RT of the test bacterium. However, as is evident from the claim, the test cannot possibly call for this. The test utilizes total RNA from the bacterium, which RNA does not have enzymatic capability. Therefore, the RT must be an extraneously added RT. The extraneously added RT will produce radiolabelled msDNA only if msDNA is present in the total RNA of the bacterium.

The significance of the test in terms of the present invention is that, if msDNA is present in the total RNA of the bacterium, then the bacterium's DNA (or RNA) must code for an RT, because msDNA can only be made in vivo by means of the bacterium's own RT. Therefore, by testing for the presence of msDNA in the total RNA of the bacterium, one is testing for the presence of a reverse transcriptase.

LAW OFFICES
Weiser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

Once it has been ascertained that a bacterium has a reverse transcriptase, the reverse transcriptase may be isolated and purified by means of the method taught in the specification in Example 3, pages 39-40. This method, which teaches the isolation and purification based on RT activity (see page 40, line 5), is applicable to any bacterium which makes RT. See page 39, lines 16-17.

Accordingly, Applicants submit that claims 9-11 are fully enabled, and respectfully request the Examiner to withdraw the rejection of these claims on this ground.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-7 have been amended to remove any indefiniteness.

The Examiner stated that claim 7 is outside the boundaries of claim 1, from which it depends, because claim 1 "recites that the RT only has 4 conserved sequences". Applicants submit, however, that claim 1 calls for an RT which comprises a particular sequence. Accordingly, claim 7 properly depends from claim 1.

Moreover, the Examiner has misread claim 7 as it depends from claim 6. Claim 6 calls for the YXDD domain of the RT to be in subdomain 5 shown in Figure 14. Claim 7 calls for the RT to have 61 conserved amino acids. It is clear that claim 7 does not call for all the 61 residues to be in the subdomain called for in claim 6.

LAW OFFICES
Welser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

The Examiner has rejected claim 8 under 35 U.S.C. §112, second paragraph, for indefiniteness. However, the Examiner has not stated any basis for the rejection of this claim on this ground. Claim 8 has been amended to clarify that the claimed RT comprises one of the sequences shown in Figure 14, which sequences are also shown in Seq. ID Nos. 30-36, respectively.

Applicants submit that the rejections of claims 1-8 under 35 U.S.C. §112, second paragraph, have been overcome and respectfully request the withdrawal of the rejections on this ground.

Rejections under 35 U.S.C. §103

I. Obviousness-type double patenting

The Examiner has rejected claims 1-10 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 5,320,958 and claims 1-7 of U.S. Patent No. 5,434,070.

Applicants will submit an appropriate terminal disclaimer at such time as the present application is allowed.

II. Rejections over prior art

The Examiner has rejected claims 1-10 under 35 U.S.C. §103 as being unpatentable over U.S. Patent Nos. 5,320,958 and 5,434,070. Applicants traverse the rejection of the claims on this ground.

The present application is a continuation-in-part of both of the two cited patent references. The specification has been

LAW OFFICES
Weiser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394

amended to update the continuation data on page 1 so as to clarify that application Serial No. 07/817,430 has since issued as U.S. Patent No. 5,434,070. Therefore, these patents are not properly citable prior art against the present invention.

The Examiner is requested to withdraw the rejection of the claims on this ground.

Conclusion

Applicants submit that the rejections of the claims has been overcome and that the claims, as amended, are in condition for allowance. An early notice to that effect is respectfully requested.

Respectfully submitted,

Howard Eisenberg

HOWARD M. EISENBERG
Weiser & Associates, P.C.
Attorney for Applicants

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER OF PATENTS AND TRADEMARKS, WASHINGTON, D.C. 20231, ON

Maureen Rainey

6-5-96 Maureen Rainey
DATE SIGNATURE

LAW OFFICES
Weiser & Associates, P.C.
SUITE 500
230 SO. FIFTEENTH ST.
PHILADELPHIA, PA 19102
(215) 875-8383
FACSIMILE (215) 875-8394